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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 09/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/989,674	WOODS, GORDON L.	
	Examiner	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-25,61 and 64-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-25, 61, and 64-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's amendment and response filed on June 17, 2004 wherein claims 1-19, 26-60, and 62-63 are cancelled; claims 20-25 and 61 have been amended; claims 64-68 are newly submitted.

Currently, claims 20-25, 61, and 64-68 are pending in this application.

Claims 20-25, 61, and 64-68 as amended now are examined on the merits herein.

Applicant's amendment amending claims 20-25 and 61, filed June 17, 2004 with respect to the rejection made under 35 U.S.C. 112 first paragraph for lack of scope of enablement for "a method of balancing the concentration of cadmium in body fluids an tissue of a human" of record stated in the Office Action dated February 27, 2004 has been fully considered and is found persuasive to overcome the rejection since the recitation "balancing" have been removed from the claims. Therefore, the said rejection is withdrawn.

Applicant's amendment filed June 17, 2004 with respect to the rejection of claims 20-22, 24-25 and 61 made under 35 U.S.C. 112 second paragraph for the use of the indefinite recitations, i.e., "balance", 'said unbalanced levels" and "sufficient to balance said cadmium concentration" of record stated in the Office Action dated February 27, 2004 have been fully considered and found persuasive to remove the rejection since the recitation have been deleted from the claims. Therefore, the said rejection is withdrawn.

Applicant's amendment changing the limitation to a specific amount herein in claims 20 and 61 filed June 17, 2004 with respect to the rejection claims 20 and 61 made under 35 U.S.C. 102(b) as being anticipated by Lakatos et al. (US 4225592) for reasons of record stated in the Office Action dated February 27, 2004 have been considered and are found persuasive to remove this particular rejection. Therefore, the said rejection is withdrawn.

Applicant's amendment changing the limitation to a specific amount herein in claims 20 and 61 filed June 17, 2004 with respect to the rejection claims 20 and 61 made under 35 U.S.C. 102(b) as being anticipated by Cini et al. (US 5130298) for reasons of record stated in the Office Action dated February 27, 2004 have been considered and are found persuasive to remove this particular rejection. Therefore, the said rejection is withdrawn.

The following is the new ground(s) of rejection(s).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-25, 61, and 64-68 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the specific

low range of cadmium to be administered to a human by the particular route employed in the claimed method, does not reasonably provide enablement for the dose range of about 0.025 to 2 mg/day be administered to a human by the broad term "administration" which may encompass any administration routes, or even the specific amounts to administered to a human, in view of the teachings of "*Cadmium oxide*" EPA Chemical Profiles, United States Environmental Protection Agency, Washington D.C. 20460, USA, Dec. 1985. 4p, and Nordberg et al. (IARC Scientific Publications, (1992) Vol. 118, No. Cadmium in the Human Environment, pp. 293-7, PTO-892).

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a method of increasing the concentration of cadmium in body fluids a tissue of a human.

The state of the prior art: The skilled artisan would clearly acknowledge that cadmium (Cd) is a well known highly toxic element. As taught by "*Cadmium oxide*" EPA Chemical Profiles, United States Environmental Protection Agency:

"Chemical safety information sheet. Exposure limits: OSHA PEL (TWA) = 0.2mg cadmium/m|3|, ceiling limit = 0.6mg cadmium /m|3|, TWA limit for cadmium oxide fume = 0.11mg/m|3|; ACGIH (1980) TLV = 0.05mg/m|3| (dust and cadmium oxide), ceiling limit for cadmium oxide fume = 0.05mg/m|3|; IDLH (NIOSH, 1978) = 0.04mg cadmium/m|3|. Lethal exposure for man has been established at 50mg cadmium/m|3| for 1h for cadmium oxide dust and for 30min for the fume. These concentrations may be inhaled without sufficient discomfort to warn workers of exposure. Toxic effects: tracheobronchitis, pneumonitis, pulmonary oedema, kidney and lung damage". (emphases added).

Thus, whether the dose range herein be administered to a human by any administration routes is safe and not toxic, is deemed to be in question and also at stake to a skilled artisan. Therefore, the dose range herein and specific administration route are considered to be an essential and critical element of the claimed invention.

The predictability of the art:

Note that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. As discussed above, cadmium (Cd) is a well known highly toxic element.

Moreover, Nordberg et al. article entitled with "*Cadmium, metallothionein and renal tubular toxicity*" teaches that:

"Cadmium-induced nephrotoxicity develops at cadmium concns. in the renal cortex of 10-300 mu.g/g wet wt. The actual concn. at which it develops depends on a no. of factors, e.g., exposure route, chem. species of cadmium administered, rate of administration and simultaneous exposure to other metals. The role of these factors can be explained by a mechanism of cadmium nephrotoxicity in which both extracellular and intracellular metallothionein binding play an essential role" (emphasis added).

Hence, the toxicity caused by the absorption and distribution of Cd into the systemic body differs drastically depending on a number of factors, especially the route of administration. Moreover, the toxicity caused by administering Cd to a human is also known to be affected by "simultaneous exposure to other metals" according to Nordberg et al. Thus, the toxicity of Cd to a human is also dependent on the nutrition status of the recipient who administered iron, selenium and/or other metals or "simultaneous exposure to other metals" as well.

Based on the known teachings regarding the toxicity of Cd to a human, one of skill in the art would recognize that it is highly unpredictable with respect to the instant claimed method by administering Cd by any administration route to a human, the dose range herein, in particular, up to 2 mg/day, is deemed to be highly unpredictable.

The amount of direction or guidance presented and the presence of absence of working examples:

Note that only a single man (fifty-five year old) was tested to administer Cd in the range of 0.25-2 mg/day, orally, parenterally or in inhalation (see page 47 of the specification). Thus, the specification is unclear as to how much of Cd to be administered to this man by which specific route either orally or parenterally or in

inhalation. As discussed above, the dose range herein and the specific administration route including orally, parenterally or in inhalation are considered to be an essential and critical element of the claimed invention. Note that the greater degree of toxicity of Cd may be encountered with parenteral administration than oral administration.

Thus, the evidence in the example is **not** commensurate in **scope** with the claimed invention and does not demonstrate criticality of a claimed range of dose and administraton route in the claimed methods. See MPEP § 716.02(d).

Thus, the specification fails to provide sufficient support as to how to practice the claimed method. As a result, necessitating one of skill to perform an exhaustive search and *undue experimentation* for the embodiments encompassed by the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factor and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation*, with no assurance of success.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20, 24, 61, and 65-67 are rejected under 35 U.S.C. 102(b) as being anticipated by Jacobson et al. (BRITISH JOURNAL OF NUTRITION, (1977 Jan) 37 (1) 107-26, of record).

Jacobson et al. discloses that twenty trace elements such as silver, arsenic, gold, bromine, **cadmium (Cd)**, cobalt, chromium, caesium, copper, iron, mercury, lanthanum, molybdenum, rubidium, antimony, scandium, selenium, samarium, tungsten and zinc, in salts, as nutrition, are administered to a human (patients) by parenteral or intravenous, in order to correcting the negative balances (or deficiency) of these trace elements such as cadmium in the said human body (see abstract, Table 1 and "Experimental" at page 108, "Subjects": human subjects tested, at page 110, the 3rd paragraph at page 111). Jacobson et al. also discloses the known amounts of Cd to be administered daily, 50-60 μg (equal to 0.05-0.06 mg) or 5-68 μg (within the instantly claimed range, see page 121 the last paragraph to the third paragraph of page 122). Jacobson et al. also points out that "The administration of trace elements is recommended in long-term total parenteral nutrition". See abstract in particular. Jacobson et al. discloses the method for determining the corresponding balance values of these trace elements in a human body by analyses for trace elements made with the aid of an ion-exchange technique based on neutron activation, and combined with subsequent gamma spectrometry (see abstract and Table 5).

Thus, Jacobson et al. anticipates Claims 20, 24, 61, and 65-67.

Response to Argument

Applicant's remarks filed June 17, 2004 with respect to the rejection made under 35 U.S.C. 102(b) as being anticipated by the same reference in the previous Office have been fully considered but they are not deemed persuasive to render the claimed invention patentable over the prior art as further discussed below.

Contrary to Applicant's assertion that the 50-60 μg (equal to 0.05-0.06 mg) or 5-68 μg of Cd is a mis-reading, the reference clearly teaches that the amount of Cd is known in the art by citing several prior art (see page 122 therein).

Moreover, Jacobson's method steps are same as the instant method steps, administering the same compound in the same amount to the same or similar patient population. See *Ex parte Novitski*, 26 USPQ 2d 1389, 1391 (Bd. Pat. App. & Int. 1993). Thus, Jacobson et al. anticipates Claims 20, 24, 61, and 65-67.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21-22, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobson et al. or Lakatos et al. (US 4225592, of record)

The same disclosure of Jacobson et al. has been discussed in the 102(b) rejections set forth above.

Lakatos et al. teaches that trace elements such as cadmium (Cd), copper, iron, and zinc, are well known to be administered to a human as nutrition (see col.9 lines 25-46). It is noted that the teachings regarding the administration of these trace elements in Lakatos et al. have been cited from several prior art references (see col.9 lines 21-46). The prior art does not expressly disclose the particular unbalance levels of cadmium in a human and the particular cadmium salt to be administered.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine the unbalanced levels of cadmium in a human and to determine the particular pharmaceutically acceptable cadmium salt to be administered in order to increase the concentration of cadmium in body fluids and tissues of a human suffering from unbalanced levels of cadmium in his body fluid and tissues and for correcting a cadmium deficiency in a human suffering therefrom.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine the unbalanced levels of cadmium in a human and to optimize the daily dose of cadmium to be administered in a methods of increasing the concentration of cadmium in body fluids and tissues of a human suffering from unbalanced levels of cadmium in his body fluid and tissues and for correcting a cadmium deficiency in a human suffering therefrom, since the method of determining the levels of trace elements in a human body is known according to Jacobson. The determination of the particular pharmaceutical acceptable cadmium salt to be administered, is considered well within conventional skills in pharmaceutical science, involving merely routine skill in the art.

Applicant's remarks filed June 17, 2004 with respect to this rejection made under 35 U.S.C. 103(a) of record in the previous Office Action have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art for the following reasons. These remarks are believed to be adequately addressed by the 102(b) rejection presented above.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703.872.9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Anna Jiang, Ph.D.
Primary Examiner, AU 1617
September 17, 2004